Spontaneous Preterm Birth Prediction in high-risk women with intervention

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In Essence

• Preterm Surveillance Clinic at St Thomas’ Hospital, London

• Prediction →
  • Identifying those at highest risk of early delivery in order to appropriately target prophylactic or reactive intervention

• How do these interventions have an impact on subsequent prediction? Can we rely on predictive markers in this setting?
qfFN and CL
Prophylactic Interventions

Transabdominal cerclage

Low transvaginal cerclage

High transvaginal cerclage
The Treatment Paradox

Traditional/Pre-Intervention Paradox

- Intervening based on a predictive marker will have an effect on outcome
- Effective intervention may reduce risk, and will make the previous test look like a poor predictor

Post-Intervention Paradox

- The presence of the intervention itself could have an impact on predictive ability
Research Questions

To what extent do prophylactic interventions have an impact on the ability of qfFN and CL to predict risk of spontaneous preterm birth?

Does the interpretation of test results need to be adjusted for the intervention?
Methods

Planned analysis of prospectively collected data from high-risk asymptomatic women

Women were classified according to prophylactic intervention cerclage OR cerclage and progesterone

qfFN and CL measurements were analysed PRE- and POST-intervention
Inclusion and Exclusion

Whole Cohort
n = 2344

Exclusions:
- Iatrogenic PTB
- Missing qfFN or CL
- Multiple Pregnancy
- Fetal Congenital Abnormality
- Incomplete outcome data

Pre-Intervention
167
18⁺0 – 21⁺6

cerclage
cerclage and progesterone

Post-Intervention
287
22⁺0 – 27⁺6

Cerclage (n=236)
cerclage and progesterone (n=51)

qfFN and CL
QUIPP App Analysis

sPTB <34 weeks of gestation (150, 7%)
Methods

Primary outcome was sPTB <34 weeks’ gestation

Diagnostic Tests

Overall Accuracy of predictive markers

- AUC of Receiver Operating Characteristic curves
Results:

1. Pre-Intervention
CERVICAL LENGTH
Accuracy of Predictive Markers Pre-Intervention

The diagnostic accuracy of CL was no better than chance
Not dependent on type of intervention used
FETAL FIBRONECTIN
Accuracy of Predictive Markers Pre-Intervention

Cerclage & progesterone
[AUC 0.47 (95% CI 0.10 to 0.84)]

Cerclage
[AUC 0.48 (95% CI 0.26 to 0.71)]

The diagnostic accuracy of fFN was no better than chance
Not dependent on type of intervention used
Results:

1. Pre-Intervention

2. Post-Intervention
CERVICAL LENGTH
Accuracy of Predictive Markers Post-Intervention

The predictive accuracy of these tests is comparable to published literature.
FETAL FIBRONECTIN

Accuracy of Predictive Markers Post-Intervention

qfFN was predictive of sPTB < 34 weeks

Cerclage & progesterone

Cerclage

[AUC 0.72 (95% CI 0.63 to 0.80)]

[AUC 0.72 (95% CI 0.54 to 0.89)]
qfFN provides clinical utility across the range of detection (0-500 ng/mL).

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<thead>
<tr>
<th>Sensitivity (%)</th>
<th>10 or greater</th>
<th>50 or greater</th>
<th>200 or greater</th>
<th>500 or greater</th>
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</thead>
<tbody>
<tr>
<td>Cerclage</td>
<td>85.4 (70.8 – 94.4)</td>
<td>58.5 (42.1 – 73.7)</td>
<td>39.0 (24.2 – 55.5)</td>
<td>17.1 (7.2 – 32.1)</td>
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<tr>
<td>Cerclage and progesterone</td>
<td>100.0 (69.2 – 100.0)</td>
<td>80.0 (44.4 – 97.5)</td>
<td>50.0 (18.7 – 81.3)</td>
<td>10.0 (0.3 – 44.5)</td>
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<thead>
<tr>
<th>Specificity (%)</th>
<th>Cerclage</th>
<th>Cerclage and progesterone</th>
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<tbody>
<tr>
<td></td>
<td>39.4 (21.0 – 48.3)</td>
<td>89.4 (82.8 – 94.1)</td>
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<td>68.2 (59.5 – 76.0)</td>
<td>98.5 (94.6 – 99.8)</td>
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<td>84.8 (68.1 – 94.9)</td>
<td>97.0 (84.2 – 99.9)</td>
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Conclusion

- Once intervention has been performed, the test is no longer predictive, suggesting that intervention reduces risk.

- Both qfFN and CL appear to be reliable predictors of sPTB < 34 weeks, even following intervention.
Discussion

Women can be reassured intervention can reduce their risk of preterm birth.

This study highlights the importance of repeat testing post intervention.

- Tests are accurate
- Helpful in planning management
- May improve morbidity & mortality for babies born too early
- Clinicians can rely on markers to reassure patients post intervention
Jenny and Kodi

Seen fortnightly

LONG cervix on TVUS

At 18 weeks:

HIGH fetal fibronectin

BED REST

SHORT cervix – STITCH

HOSPITAL ADMISSION

Post-stitch, CL stable; fetal fibronectin HIGH

Early referral

2 x LM

28+1
Acknowledgements

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• Dr Alex Ridout
• Mr Paul Seed
• Dr Rachel Tribe
• Dr Helena Watson
• There is a Treatment Paradox in this group of women
• The QUiPP App is a safe and accurate risk prediction tool both with and without intervention, at early and late gestations